

Rec'd PCT/PTO 24 AUG 2004  
PCT/GB 2003 / 0 0 0 8 4 3



INVESTOR IN PEOPLE

The Patent Office  
Concept House  
Cardiff Road  
Newport  
South Wales  
NP10 8QQ

## PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN  
COMPLIANCE WITH RULE 17.1(a) OR (b)

REC'D 25 MAR 2003

WIPO

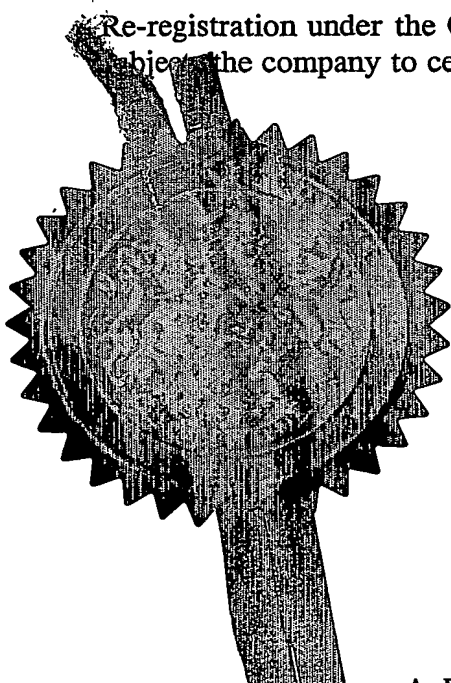
PCT

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.



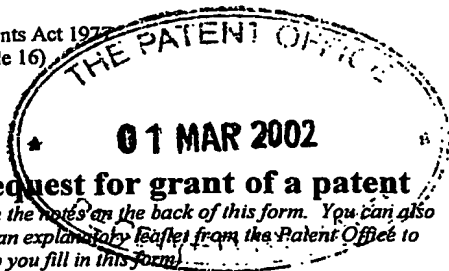
*R. Mahoney*

Signed

Dated 18 March 2003

**Patents Form 1/77**

Patents Act 1977  
(Rule 16)



**The  
Patent  
Office**

04MAR02 E700329-1 010005  
P01/7700 0.00-0204919.5

**The Patent Office**

Cardiff Road  
Newport  
South Wales  
NP9 1RH

**Request for grant of a patent**

*(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form.)*

1. Your reference	RGC/P10970.2GB		
2. Patent application number <i>(The Patent Office will fill in this part)</i>	01 MAR 2002	<b>0204919.5</b>	
3. Full name, address and postcode of the or of each applicant <i>(underline all surnames)</i>	CST MEDICAL LIMITED 2A BRIDGE STREET SILSDEN KEIGHLEY WEST YORKSHIRE BD20 9NB  08335861001 Patents ADP number <i>(if you know it)</i>  If the applicant is a corporate body, give the Country/state of its incorporation UNITED KINGDOM		
4. Title of the invention	TREATMENT OF FEMALE SEXUAL DYSFUNCTION		
5. Name of your agent <i>(if you have one)</i>	OLSWANG		
"Address for service" in the United Kingdom to which all correspondence should be sent <i>(including the postcode)</i>  Patents ADP number <i>(if you know it)</i>	90 LONG ACRE LONDON WC2E 9TT  07627995001		
6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and <i>(if you know it)</i> the or each application number	Country	Priority application number <i>(if you know)</i>	Date of filing <i>(day / month / year)</i>
7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application	Date of filing <i>(day / month / year)</i>	
8. Is a statement of inventorship and of right to grant of a patent required in support of this request? <i>(Answer 'Yes' if:</i> a) <i>any applicant named in part 3 is not an inventor, or</i> b) <i>there is an inventor who is not named as an applicant, or</i> c) <i>any named applicant is a corporate body.</i> See note (d))	YES		

## Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form

Description

9

Claim(s)

Abstract

Drawings

- 
10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (*Patents Form 7/77*)

Request for preliminary examination and search (*Patents Form 9/77*)

Request for substantive examination (*Patents Form 10/77*)

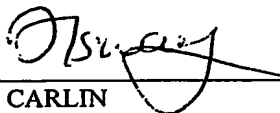
Any other documents  
(*please specify*)

---

11.

I/We request the grant of a patent on the basis of this application.

Signature



Date 1 MARCH 2002

- 
12. Name and daytime telephone number of person to contact in the United Kingdom

ROBERT CARLIN  
020 7208 8888

---

### Warning

*After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.*

## TREATMENT OF FEMALE SEXUAL DYSFUNCTION

The present invention relates to the treatment of female sexual dysfunction and is directed particularly, but not exclusively, to Hypoactive Sexual Desire Disorder.

The term female sexual dysfunction is a term used for various disorders of the sexual process in women and is categorised by pain associated with intercourse or by a disturbance in the process that forms the sexual response cycle. The sexual response cycle is divided into four distinct phases consisting of (i) the desire phase; (ii) the arousal or excitement phase; (iii) the orgasmic or plateau phase; and (iv) the resolution phase.

The (i) desire phase involves fantasies about and the desire to have sexual activity. The lack of such fantasies and desires and the general lack of receptivity to sexual activity is referred to as Hypoactive Sexual Desire Disorder (HSDD). This disorder may cause personal distress or interpersonal difficulties.

The (ii) arousal or excitement phase is typically evidenced by vaginal lubrication as a consequence of increased fluid production through blood flow. Dysfunction in this cycle is termed Sexual Arousal Disorder and manifests itself as an inability to obtain or maintain sufficient and adequate vaginal lubrication or a swelling response during this phase. This disorder is commonly associated with post-menopausal women and may cause extreme personal distress and interpersonal difficulties. That said, all women may be affected by this disorder at some stage in their lives.

The final phase, (iv) the resolution phase, is when the blood flow returns to normal and muscle tension and tightness dramatically decrease.

There are further forms of sexual dysfunction, such as female orgasmic disorder which is described as a persistent or recurrent delay or absence of an orgasm following the normal sexual excitement phase. This disorder may be present in women as a result of surgery or hormone deficiencies and/or present in women who have never achieved an orgasm.

Additionally, there are sexual pain disorders and these generally fall into one of two categories. The first category is dyspareunia and concerns genital pain associated with sexual intercourse. Pain can be associated with initial penetration or during deep thrusting, resulting in an intensity of pain which makes the prolonging of intercourse near impossible. The other category of sexual pain disorder is vaginismus and this is defined as the recurrence or persistent involuntary spasm or contraction of the perineal muscles that surround the outer third of the vagina when the insertion of any object is attempted.

The female sexual dysfunction which is of principal concern to the present invention is the treatment of Hypoactive Sexual Desire Disorder (HSDD). Of all female sexual problems, a lack of interest in sexual activity is most prevalent, affecting 30% of women.<sup>1</sup>

HSDD concerns sexual desire and this desire has two main manifestations - "proceptivity" (seek out and/or initiate sexual activity) and "receptivity" (accept sexual activity when offered). These manifestations are analogous to an appetite for food, the analogy being that when we feel hungry we seek out food, or when we do not feel hungry we do not seek out food until we see it tasteful and attractively presented. For many women, the complaint of lack of sexual desire is found, typically, to mean a lack of proceptivity, the woman maintaining receptive sexual behaviour.

Indeed the "appetite" phase of sexual functioning can be conceptualised in two components - designated "sexual drive" and "sexual desire".<sup>2</sup> In this dichotomisation, the term "sexual drive" means the biological drive that generates proceptivity and receptivity. This drive is omnipotent in that it can be satisfied by a variety of behaviour (e.g. sexual activity with a partner, masturbation, sexual fantasies). Conversely, the term "sexual desire" is used to mean a desire for a specific behaviour. In effect, "sexual desire" is focused sexual drive.

It will be appreciated that the physiology of sexual drive in women is not well understood. Sexual drive is thought to be generated in specific nuclei of the hypothalamus, often called

---

<sup>1</sup> Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States. *JAMA* 1999; 281: 537-544.

<sup>2</sup> Riley A. Problems of the sexual response cycle. *The Diplomat, The Journal of the Diplomats of the Royal College of Obstetricians and Gynaecologists*, 1997; 4: 270-275.

collectively the "sex drive centre". These nuclei have positive (sexually enhanced) and negative (sexually inhibiting) influences from other centres of the central nervous system mediated through neurotransmitters and neurohormones.

Treatment of HSDD may be two fold. Firstly and importantly, a correct diagnosis of HSDD would need to be made. Once a physician is comfortable that there is no organic cause and that any severe medical conditions, such as diabetes or heart disease, were correctly treated, it would then be necessary to discuss interpersonal difficulty with a partner. Once HSDD is diagnosed, the condition would be amiable to treatment with sexual therapy. A further treatment may be by hormone therapy.

Oestrogen therapy is commonly used in the pharmacological treatment of sexual dysfunction in women. Oestrogen-based therapies are generally used to increase mucus production, to provide vasodilatory effects, or to increase the general health of the vagina.<sup>3</sup> In such treatments, oestrogen is administered orally, by injection or topically. With oral administration, the oestrogen concentration encountered by the liver is generally four to five times greater than the oestrogen levels in peripheral blood. This effect may lead to an undesirable increase in the production of certain coagulation factors and renin substrates in the liver. Oestrogen administered by injection avoids this effect in the liver. However, all oestrogen-based therapies are known to increase the risk of endometrial hyperplasia, endometrial cancer and breast cancer in treated individuals. Due to the increased risk of endometrial hyperplasia and endometrial cancer encountered with oestrogen therapies, the use of oestrogen/progestogen combinations have been utilised. However, these have the common side effects of inducing uterine bleeding and the continuation of menstrual periods.

Alternatively, male hormones collectively known as androgens, such as testosterone, and the lack of these in the female body have been linked to forms of sexual dysfunction. Testosterone is produced in a woman's body and the pinnacle of production is generally around the woman's reproductive years. This production can wane for a variety of reasons

---

<sup>3</sup> Nadelson et al., eds., *Treatment Interventions in Human Sexuality* (New York: Plenum Press, 1983)

and this waning can be counter-acted in certain instances by testosterone replacement therapy. In certain cases this counter-acting effect has prompted an increase in sex drive.

Nevertheless, testosterone replacement therapy carries with it several dangers analogous to oestrogen replacement therapy and as such is far from satisfactory.

Accordingly, it is a general aim of the present invention to provide a treatment female sexual dysfunction and delivery method for said treatment, and specifically the treatment of HSDD, which overcomes or ameliorates the problems and drawbacks associated with the prior art as well as, preferably, overcoming other apparent problems and drawbacks with medicaments for female sexual dysfunction in general.

According to a first aspect of the present invention, there is provided an aroma which is characterisable and is capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD. The use of an aroma is advantageous since it is capable of acting directly on the brain without having to pass through the blood brain barrier which is in stark contrast to medicaments which are typically administered by ingestion or intravenously.

The aroma of the present invention most preferably comprises erogenic aromatic molecules which affect the olfactory system of the brain. The aroma of the present invention may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

Desirably said carboxylic acids exhibit paradoxical aroma profiles, wherein these profiles combine reassuring odour notes of warm human flesh but wherein said odour notes are embedded in distinctly fruity odour notes, these odour notes can often serve to prevent the conscious mind apprehending the occult, erogenic odour note. Furthermore said aldehydes may additionally comprise new synthetic aldehydes which can exhibit a floral odour note with a heart of erogenicity.

According to a second aspect of the present invention, there is provided a range of compounds which are capable of effecting a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly ameliorate the effects of HSDD. The compounds of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These compounds may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a third aspect of the present invention, there is provided a medicament comprising a range of compounds, wherein said compounds are capable of effecting a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD. The compounds of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These compounds may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a fourth aspect of the present invention, there is provided a set of formulations which are capable of effecting a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD. The formulations of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These formulations may be composed such that they comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.



According to a fifth aspect of the present invention, there is provided a medicament comprising a set of target formulations wherein said formulations are capable of effecting a physiological effect in or from the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD. The formulations of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These formulations may be composed such that they comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a sixth aspect of the present invention, there is provided a medicament for application to a patient in avoidance of the human blood brain barrier, wherein said medicament is capable of effecting a physiological effect in or from the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD. The medicament of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These medicaments may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a seventh aspect of the present invention, there is provided a compound or compounds possessing an appropriate molecular size and electrical charge to interact with a neuroreceptor in the human brain in such a way as to have an agonistic effect in order to cause the emission of neurotransmitters which cause an effect to the central nervous system, said effect being a physiological effect which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD. The compound(s) of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These compound(s) may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules,

including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to an eighth aspect of the present invention, there is provided a formulation or formulations possessing an appropriate component of the formulation which is capable of interacting with a neuroreceptor in such a way as to have an agonistic effect in order to cause the emission of neurotransmitters which cause an effect to the central nervous system, said effect being a physiological effect which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD. The formulation(s) of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These formulation(s) may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a ninth aspect of the present invention, there is provided a dopaminergic agonist(s) which is capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD. The dopaminergic agonist(s) of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. These dopaminergic agonist(s) may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a tenth aspect of the present invention, there is provided a natural human odorant which is characterisable and/or a synthetic human odorant which is characterisable and is capable of causing a physiological effect in or from the human brain which causes the

amelioration of female sexual dysfunction, and particularly the amelioration of HSDD. The odorants of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain.

According to an eleventh aspect of the present invention, there is provided a medicament in the form of an aroma wherein said aroma has been masked or disguised such that the component aroma contained therein is not immediately apparent on application to the patient, yet said aromas are capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual disorder, and particularly the amelioration of HSDD. The aroma of the present invention which has been masked or disguised ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. This aroma may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

According to a twelfth aspect of the present invention, there is provided an aroma which has a pre-determined character as defined by an electronic nose, wherein said aroma is capable of causing a physiological effect in or from the human brain which causes the amelioration of female sexual dysfunction, and particularly the amelioration of HSDD. The aroma of the present invention ideally comprises erogenic aromatic molecules which affect the olfactory system of the brain. The aroma of the present invention may comprise at least one of the following groups of compounds: steroid odorants; amines and related molecules; heterocyclic aroma molecules, including those at the heart of erogenic Jasmin oil; aromatic molecular mimics of the central neurotransmitter dopamine; carboxylic acids including those which may occur in trace levels in human secretions; aldehydes, including those which form trace ingredients in odorous human secretions.

The aforementioned aspects of the present invention describe the “active ingredient(s)” of the present invention. The aspects of the invention mentioned hereinafter describe the delivery systems of the present invention for administration of the “active ingredient(s)” to a patient.

According to a thirteenth aspect of the present invention, there is provided a delivery system for any of the "active ingredient(s)" of the present invention to the patient in the form of a nasal spray. The nasal spray may be administered to the patient by a medical practitioner or by the patient themselves. The "active ingredient(s)" may be present in as a fluid in an appropriate concentration to be administered to the patient by the form of said nasal spray. Said nasal spray can comprise a reservoir inoperative connection with a pump action spray nozzle. The fluid can be housed in a reservoir of the nasal spray until it is to be administered to a patient. It is preferably envisaged that the nasal spray will be placed in or near the nasal cavity/cavities of the patient to facilitate administration of the "active ingredient(s)".

According to a fourteenth aspect of the present invention, there is provided delivery system in the form of a patch which is to be worn by the patient which is coated or impregnated with the "active ingredient(s)". Typically, the patch is adhered to the skin of the patient to allow the "active ingredient(s)" to be emitted therefrom and into the patient via their nasal cavities. Such patches are available from The Aromacology Patch Company.

Alternatively, the patch or a strip of patch material may be housed in a protective sheath, such as a plastic sheath, to allow the insertion of same into the nasal cavities of the patient, such that the patient may draw the active ingredient of the present invention into their nasal cavities via an inhalation of breath through their nasal cavities. It is to be appreciated that the appropriate concentrations of the "active ingredient(s)" are to be used in the patch delivery system and may be included with any other suitable agent to facilitate the release of said "active ingredient(s)" into the nasal cavity/cavities of the patient.

According to a fifteenth aspect of the present invention, there is provided a delivery system for the "active ingredient(s)" of the present invention which may be applied topically to the patient for inhalation via the nasal cavities of the patient. Such topical applications could be provided in the form of a lipstick or perfume or any other suitable means which are to be applied to the skin and which are capable of being inhaled by the patient via their nasal cavities.